

What is claimed is:

1. An isolated nucleic acid molecule which encodes an agonist polypeptide antigen derived from MUC-1, wherein the agonist polypeptide stimulates an immune response.
2. The nucleic acid molecule of claim 1, wherein the agonist polypeptide binds to HLA molecules with a high avidity.
3. The nucleic acid molecule of claim 1, wherein the agonist polypeptide has a higher association constant (K_a) for the HLA than a native polypeptide.
4. The nucleic acid molecule of claim 1, wherein the agonist polypeptide has a lower dissociation constant (K_d) for the HLA than a native polypeptide.
5. The nucleic acid molecule of claim 1, which encodes an agonist polypeptide up to about 12 amino acids in length.
6. The nucleic acid molecule of claim 1, wherein the agonist polypeptide is derived from a mucin tumor antigen.
7. The nucleic acid molecule of claim 1, wherein the agonist polypeptide is derived from a non-variable number of tandem repeats region of MUC-1.
8. The nucleic acid molecule of claim 1, wherein the immune response is a cellular immune response.
9. The nucleic acid molecule of claim 8, wherein the cellular immune response is a cytotoxic T cell response.
10. The nucleic acid molecule of claim 8, wherein the cellular immune response is a T helper cell response.
11. The nucleic acid molecule of claim 8, wherein the cellular immune response is a B cell immune response.

12. The nucleic acid molecule of claim 1, comprising a nucleic acid sequence corresponding to any one of the amino acid sequences as identified by SEQ ID NO: 1 through 19, fragments or variants thereof or to SEQ ID NO: 19 through 37, fragments or variants thereof.

13. The nucleic acid molecule of claim 1, comprising a nucleic acid sequence corresponding to the amino acid sequence as identified by SEQ ID NO: 19, or fragments thereof or to SEQ ID NO: 19 through 37, fragments or variants thereof.

14. An isolated polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 1 through 19, fragments or variants thereof.

15. An isolated polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 1, fragments or variants thereof.

16. The isolated polypeptide of claim 14, wherein the polypeptide comprises SEQ ID NO: 19, fragments or variants thereof.

17. The isolated polypeptide of claim 14, wherein the polypeptide binds to HLA molecules with a high avidity.

18. The isolated polypeptide of claim 14, wherein the polypeptide has a higher association constant (K_a) for the HLA than a native polypeptide.

19. The isolated polypeptide of claim 17, wherein the polypeptide has a lower dissociation constant (K_d) for the HLA than a native polypeptide.

20. The isolated polypeptide of claim 17, wherein the polypeptide is derived from a mucin tumor antigen.

21. The isolated polypeptide of claim 17, wherein the polypeptide is derived from a non-variable number of tandem repeats region of MUC-1.

22. The isolated polypeptide of claim 17, wherein the polypeptide induces an immune response.

23. The isolated polypeptide of claim 17, wherein the immune response is a cellular immune response.

24. The isolated polypeptide of claim 23, wherein the cellular immune response is a cytotoxic T cell response.

25. The isolated polypeptide of claim 23, wherein the cellular immune response is a T helper cell response.

26. The isolated polypeptide of claim 23, wherein the cellular immune response is a B cell immune response.

27. An agonist polypeptide comprising an amino acid sequence which is at least about 60% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

28. An agonist polypeptide comprising an amino acid sequence which is at least about 80% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

29. An agonist polypeptide comprising an amino acid sequence which is at least about 90% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

30. An agonist polypeptide comprising an amino acid sequence which is up to about 99.9% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

31. A method for generating an immune response to a MUC-1 tumor antigen comprising administering an isolated nucleic acid molecule in a therapeutically effective dose sufficient to generate a cellular immune response, wherein the isolated nucleic acid molecule encodes any one or more of polypeptides identified by SEQ ID NO: 1 through 19.

32. The method of claim 31, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 60% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

33. The method of claim 31, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 80% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

34. The method of claim 31, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 90% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

35. The method of claim 31, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 99.9% identical to the amino acid sequence of SEQ ID NO: 1 through 19.

36. The method of claim 31, wherein the isolated nucleic acid molecule comprises a vector encoding any one or more of amino acid sequences identified by SEQ ID NO: 1 through 19.

37. The method of claim 31, wherein the isolated nucleic acid molecule comprises a vector encoding a polypeptide identified by SEQ ID NO: 19.

38. The method of claim 37, wherein an immune response is generated against a MUC-1 tumor.

39. The method of claim 31, wherein the immune response is a cytotoxic T cell response.

40. A nucleic acid vector comprising one or more nucleic acid sequences encoding polypeptides identified by any one or more of SEQ ID NO: 1 through 19, operably linked to an inducible promoter.

41. The nucleic acid vector of claim 40, wherein the vector is a viral vector.
42. The nucleic acid vector of claim 40, wherein the vector is a plasmid.
43. The nucleic acid vector of claim 40, wherein the inducible promoter is tissue specific.
44. A recombinant vector comprising a nucleic acid sequence encoding any one of the polypeptides identified by SEQ ID NO: 1 through 19.
45. A host cell comprising a vector of any one of claims 40 through 44.
46. A method for treating a subject suffering from or susceptible to a MUC-1 tumor comprising administering to a subject any one or more of the peptides identified by SEQ ID NO: 1 through 19.
47. The method of claim 46, wherein the subject is treated by administering a peptide which is at least about 60% identical to any one or more of the amino acid sequences identified by SEQ ID NO: 1 through 19.
48. The method of claim 46, wherein the subject is treated by administering a peptide which is at least about 80% identical to any one or more of the amino acid sequences identified by SEQ ID NO: 1 through 19.
49. The method of claim 46, wherein the subject is treated by administering a peptide which is at least about 90% identical to any one or more of the amino acid sequences identified by SEQ ID NO: 1 through 19.
50. The method of claim 46, wherein the subject is treated by administering a peptide which is at least about 99.9% identical to any one or more of the amino acid sequences identified by SEQ ID NO: 1 through 19.

51. A method for treating a subject suffering from or susceptible to a MUC-1 tumor comprising:
isolating dendritic cells from a subject suffering from cancer;
treating the dendritic cells with one or more of polypeptides identified by SEQ ID NO: 1 through 19; and,
administering the treated dendritic cells to the subject.
52. The method of claim 51, wherein dendritic cells are treated with one or more polypeptides at least about 60% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.
53. The method of claim 51, wherein dendritic cells are treated with one or more polypeptides at least about 80% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.
54. The method of claim 51, wherein dendritic cells are treated with one or more polypeptides at least about 90% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.
55. The method of claim 51, wherein dendritic cells are treated with one or more polypeptides at least about 99.9% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.
56. A method for generating an immune response to a weakly immunogenic antigen comprising administering to a subject a polypeptide with a high avidity for HLA fused to a weak immunogen.
57. The method of claim 56, wherein the weak immunogen is a differentiation antigen.
58. The method of claim 56, wherein the weak immunogen is a tumor antigen.

59. The method of claim 56, wherein the polypeptide comprises the HLA binding fragment of SEQ ID NO: 19.

60. The method of claim 59, wherein HLA binding fragment of SEQ ID NO: 19 is fused to a carcinoembryonic antigen.

61. The method of claim 59, wherein the HLA binding fragment of SEQ ID NO: 19 is fused to a viral antigen.

62. The method of claim 59, wherein the HLA binding fragment of SEQ ID NO: 19 is fused to a self-antigen.

63. An isolated nucleic acid molecule which encodes an agonist polypeptide antigen derived from a non-variable number of tandem repeats region of MUC-1, comprising a nucleic acid sequence corresponding to any one of the amino acid sequences as identified by SEQ ID NO: 1 or 3 - 18, fragments or variants thereof, wherein the agonist polypeptide stimulates an immune response.

64. A method of screening for a molecule to generate an immune response to a MUC-1 tumor antigen, comprising:

altering a nucleic acid encoding a portion of the non-variable number of tandem repeats of MUC-1;

expressing the altered nucleic acid to produce a molecule;

contacting a dendritic cell with the molecule; and

contacting a T-cell with the dendritic cell,

wherein a modulation of the IFN- γ production of the T-cell indicates that the molecule may generate an immune response.

65. The method of claim 64, wherein the dendritic cell is from a subject diagnosed with cancer.

66. The method of claim 64, wherein the dendritic cell after it is treated with the molecule is contacted with a peripheral blood mononuclear cell.

67. A method for treating a subject suffering from or susceptible to a MUC-1 tumor comprising:
isolating dendritic cells from a subject suffering from cancer;
treating the dendritic cells with one or more of polypeptides identified by SEQ ID NO: 1 through 19;
activating peripheral blood mononuclear cells with the treated dendritic cells;
administering the activated PBMC cells to the subject.

68. The method of claim 67, wherein dendritic cells are treated with one or more polypeptides at least about 60% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.

69. The method of claim 67, wherein dendritic cells are treated with one or more polypeptides at least about 80% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.

70. The method of claim 67, wherein dendritic cells are treated with one or more polypeptides at least about 90% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.

71. The method of claim 67, wherein dendritic cells are treated with one or more polypeptides at least about 99.9% identical to any one of the amino acid sequences identified by SEQ ID NO: 1 through 19.

72. A method for generating an immune response to a MUC-1 tumor antigen comprising administering an isolated nucleic acid molecule in a therapeutically effective dose sufficient to generate a cellular immune response, wherein the isolated nucleic acid molecule is identified by SEQ ID NO: 20 through 37.

73. The method of claim 72, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 60% identical to the amino acid sequence of SEQ ID NO: 20 through 37.

74. The method of claim 72, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 80% identical to the amino acid sequence of SEQ ID NO: 20 through 37.

75. The method of claim 72, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 90% identical to SEQ ID NO: 20 through 37.

76. The method of claim 72, wherein the isolated nucleic acid molecule encodes a polypeptide at least about 99.9% identical to SEQ ID NO: 20 through 37.

77. The method of claim 72, wherein the isolated nucleic acid molecule comprises a sequence identified by SEQ ID NO: 20 through 37.

78. The method of claim 72, wherein the isolated nucleic acid molecule comprises a vector including a sequence identified by SEQ ID NO: 19.